Regulation of Epidermal Self-Renewal and Differentiation by Histone and DNA Demethylases.

Grant Award Details

Regulation of Epidermal Self-Renewal and Differentiation by Histone and DNA Demethylases.

Grant Type: Basic Biology IV

Grant Number: RB4-05779

Project Objective: The goal of the project is to elucidate the role of epigenetic regulators (histone demethylases and mediators of DNA demethylation) in the self-renewal and differentiation of human epidermal stem cells

Investigator:

Name:	George Sen
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Skin Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: $1,080,000

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title:	Regulation of Epidermal Self-Renewal and Differentiation by Histone and DNA Demethylases.
Public Abstract:	Tissue specific stem and progenitor cells exist to replenish the tissue it resides during normal homeostasis or during regeneration from a wound. Disease and aging leads to a depletion of these stem and progenitor cells, which can impede the ability of the body to regenerate itself. Thus, an understanding of the mechanisms of how tissue specific stem and progenitor cells self-renew and differentiates is key to being able to maintain these cells for life and to use these cells therapeutically. Stem and progenitor cells reside in specific niches in our bodies, which interact with neighboring cells and extracellular proteins. Unfortunately, this type of interaction is difficult to model in cultured cells. We have previously developed methods to regenerate 3D intact human epidermis on immune compromised mice, which allows us to investigate the factors important for tissue regeneration. Potential regulators of epidermal stem cell self-renewal and differentiation include epigenetic factors. Epigenetic factors are proteins that modify either DNA or histone. Alterations in DNA or histone can lead to heritable changes in gene expression, which may lead to a stem cell determining whether to differentiate or proliferate. We propose to determine the function of modifiers of DNA and histone methylation in epidermal stem cell self-renewal and differentiation. This will lead to a fundamental understanding of how tissue specific stem cells maintain a tissue for the duration of our lives.
Statement of Benefit to California:	Millions of Californians suffer from epidermal derived skin disorders, which range from psoriasis, squamous cell carcinomas, basal cell carcinomas to chronic wounds. These diseases are characterized by abnormalities in epidermal stem and progenitor cell growth and differentiation. For example, increased proliferation and failure to properly differentiate can lead to skin carcinomas. Currently not much is known about the mechanisms that govern epidermal stem cell growth and differentiation. This proposal seeks to understand the fundamental mechanisms of epidermal stem cell self-renewal and differentiation through the study of epigenetic factors, which may yield insights in the development of therapies for epidermal disorders. Our proposed research will benefit California in several ways: 1) our research should provide epigenetic targets that can be modulated by small molecules that can potentially treat epidermal disorders; 2) provide a thorough understanding of how adult somatic stem cells regenerate tissue; 3) training the next generation of stem cell scientists.